

## MCM Update March 2024: HSD17B11

### Terminology

- **Steroidogenesis:** The process by which cholesterol is converted to various steroid hormones
- **Idiopathic non obstructive azoospermia:** The most severe type of male infertility, characterized by low testicular volume and severely low sperm concentration, with no identified cause.

### Summary

We continue to characterise lung cancer biomarkers identified in the MCM1 project. This update focuses on HSD17B11, a gene associated with lung cancer survival. HSD17B11 is a protein coding gene, relatively ubiquitously expressed across organs and tissues. It is a short-chain alcohol dehydrogenase that metabolises secondary alcohols and ketones.

### Background

Identifying molecular markers and their combination (signatures) enables us to detect disease earlier (diagnostic signatures) and stratify patients into subgroups based on disease progression patterns (prognostic signatures), potentially leading to identifying which patients may benefit from different treatment options (predictive signatures). The Mapping Cancer Markers project analyzes data sets with millions of data points collected from patients with cancers and sarcomas to find such diagnostic, prognostic and predictive signatures.

Since November 2013, World Community Grid volunteers have donated over 894,000 CPU years to the project, helping analyse data on lung and ovarian cancer and sarcoma, much more thoroughly than otherwise possible. We are immensely grateful for this continued support.

Further characterising the 26 top-scoring genes in lung cancer, we have already discussed [VAMP1](#), [FARP1](#), [GSDMB](#), [ADH6](#), [IL13RA1](#), [PCSK5](#), and [TLE3](#) in previous MCM updates. Here, we outline information on HSD17B11. Importantly, there is a strong relationship across all these proteins so far, as highlighted in Figure 1. HSD17B11 is the 4th most connected protein from our list (FARP1, TLE3, PCSK5 being more connected).

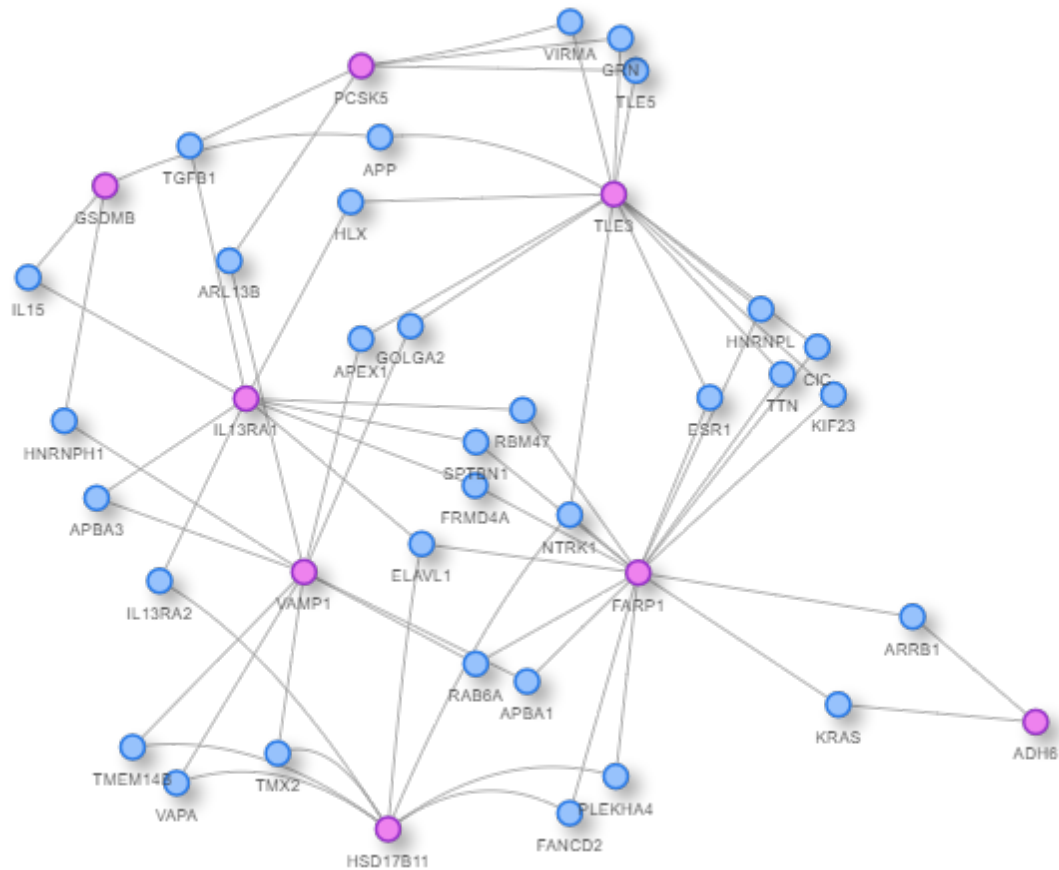


Figure 1. Physical protein interactions linking the 8 proteins we have focused on so far (pink nodes). Data from our [IID database](#).

### HSD17B11 Research

HSD17B11 is a gene that encodes a protein called hydroxysteroid 17-beta-dehydrogenase 11. Hydroxysteroid 17-beta-dehydrogenase 11 can convert androstan-3-alpha,17-beta-diol to androsterone *in vitro*, which suggests that it may participate in androgen metabolism during steroidogenesis ([Uniprot](#)). Considering its structure (Figure 2), HSD17B11 has four known ligands that can bind to it, including androsterone, glycerol, sulfate ion, and chloride ion.

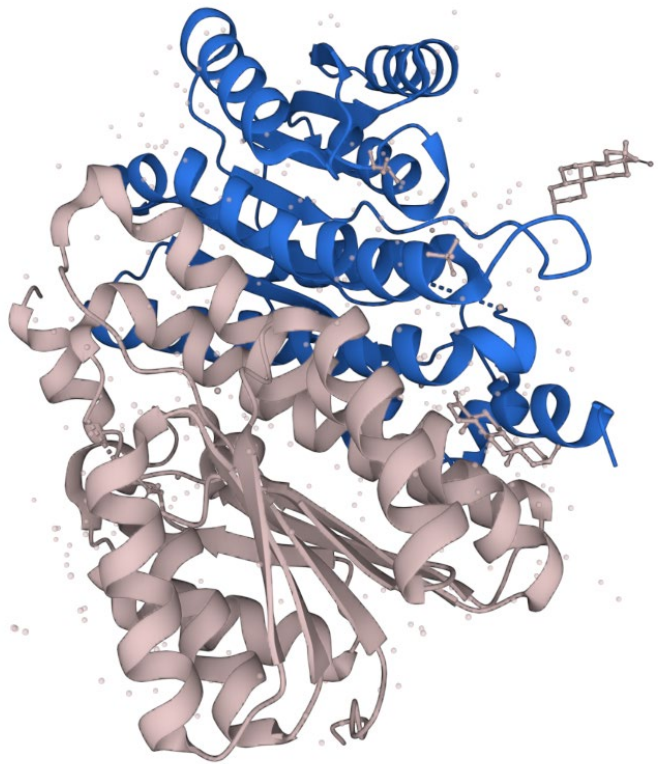


Figure 2. Protein HSD17B11 structure ([PDB](#)).

A large meta-analysis revealed that single-nucleotide polymorphisms in HSD17B11 are significantly associated with lean body mass<sup>[1]</sup>. HSD17B11 was also found to be a potential biomarker for coronary artery disease<sup>[2]</sup> and idiopathic non obstructive azoospermia<sup>[3]</sup>.

HSD17B11 was found to have a protective role in lung cancer (Figure 3), in accordance with the other genes we have presented so far.

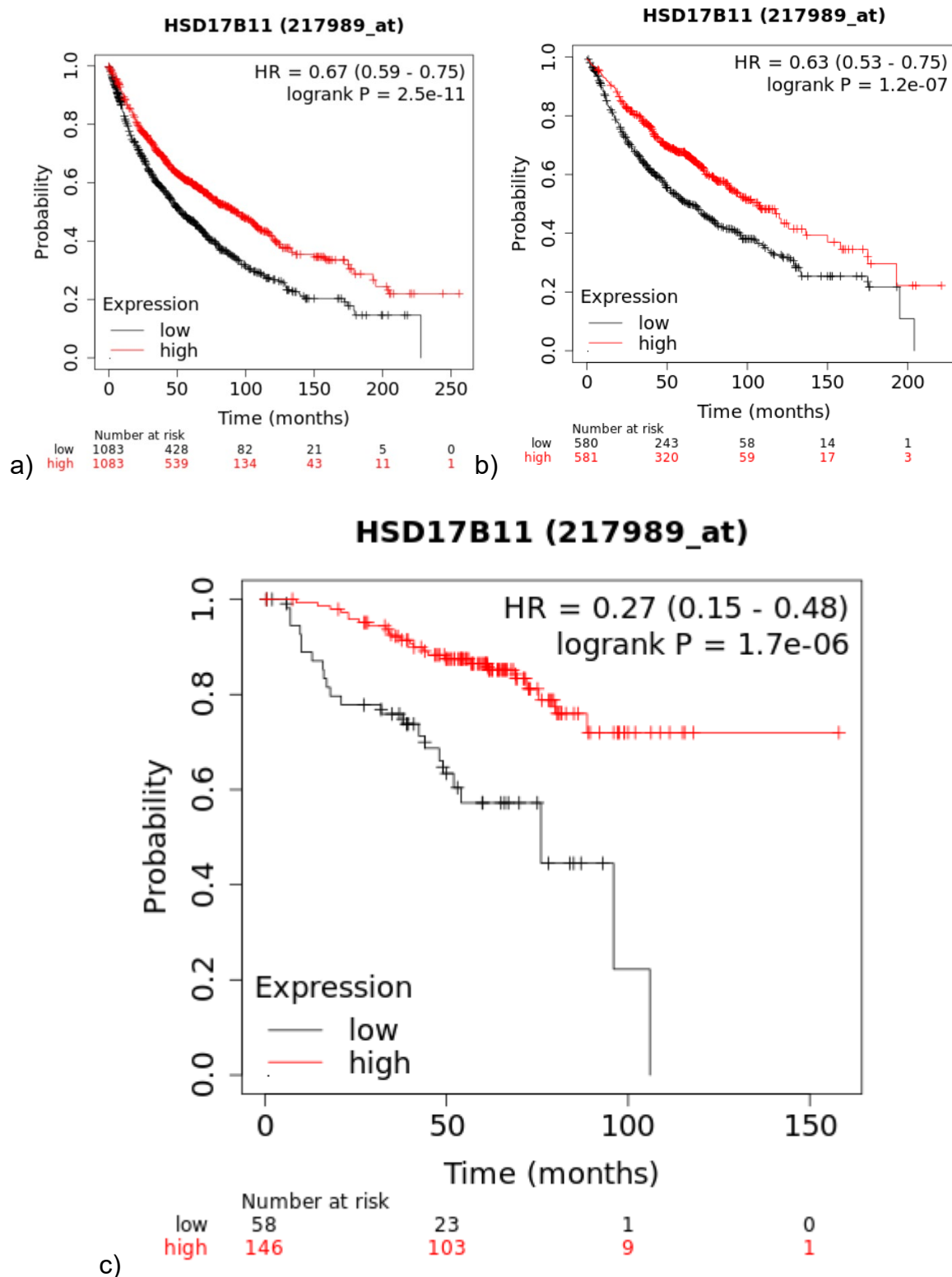


Figure 3. a) Survival curves for patients with low and high expression of HSD17B11 (KMplot). b) An even stronger association is detected for lung adenocarcinoma and c) for never smokers.

We investigated further to explore the association between HSD17B11 and other cancers. As shown in Figure 4, comparing cancer tissues and normal tissues,

HSD17B11 is differentially expressed in most cancers (indicated by red text). In most cancers, it is upregulated, except breast, colon, lung squamous cell carcinoma, ovary, renal, thyroid and uterus cancers. Within the literature, HSD17B11 has been associated with prostate cancer prognosis<sup>[4]</sup> and with survival in pancreatic cancer<sup>[5]</sup>.

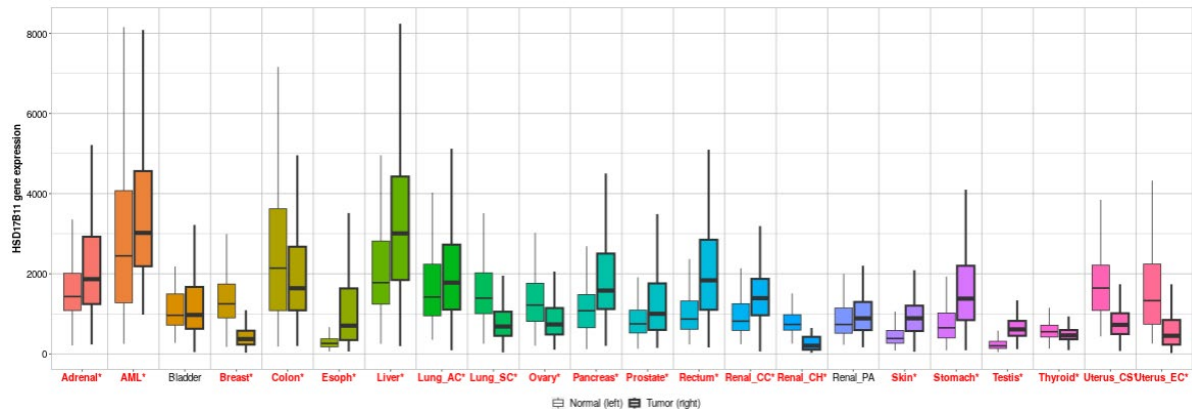


Figure 4. Expression of HSD17B11 in normal and cancer tissue for multiple cancer types. Red text represents a significant difference between expression in cancer tissue compared with normal tissue ([TNMplot](#)).

If you have any questions or comments, please leave them in this thread for us to answer!

WCG Team

## References

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